Trichomegaly of the Eyelashes After Treatment with Erlotinib in Non-small Cell Lung Cancer

Judith Elizabeth Carser, MB, BCh, MRCR, and Yvonne Jane Summers, PhD, MBChB, MRCP

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The expanding use of the epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor erlotinib in the management of patients with advanced non-small cell lung cancer has led to an interest in the early identification of those who are likely to gain benefit. We present the case of a patient with a durable clinical response, who developed trichomegaly (excessive eyelash growth) without the characteristic skin rash.

CASE REPORT

A 61-year-old female never-smoker presented with a 3-month history of increasing dyspnoea on exertion and persistent cough. Chest radiogram and computed chest tomography (CT) showed patchy infiltrates in the right mid-lower lobes, but bronchoscopy was normal, with no endobronchial lesion seen and no malignant cells in the bronchial wash. A transbronchoscopic biopsy was not performed. Repeat imaging 3 months later confirmed progressive air space consolidation, and a CT-guided fine-needle aspirate showed features in keeping with a well-differentiated mucin variant of bronchoalveolar carcinoma.

The patient's only significant medical history was hypertension and hypercholesterolaemia, for which she had been prescribed atorvastatin and propranolol.

This patient elected not to receive palliative platinum-based combination chemotherapy; therefore, the potential of erlotinib as initial therapy was discussed. Treatment commenced in April 2005, and erlotinib 150 mg daily was prescribed through an expanded access program before licensing. Within 4 weeks, there was a marked symptomatic improvement in exercise tolerance and almost complete resolution of the previous copious bronchial secretions. Radiological imaging showed static disease (Figures 1 and 2). No assessments for EGFR mutation status were performed in this patient.

During the patient's 10 months of treatment, she did not develop any significant cutaneous or gastrointestinal toxicity,

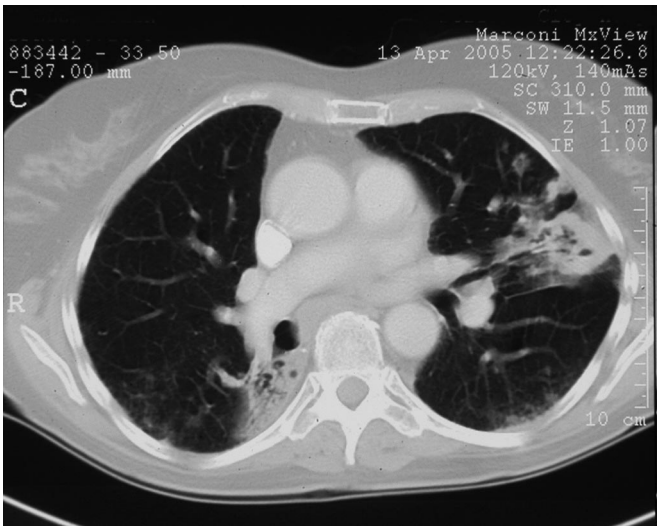

FIGURE 1. Chest computed tomographic scan before treatment.

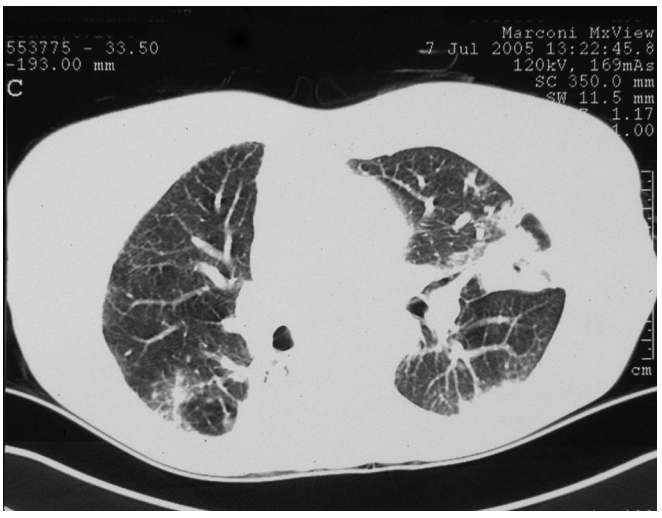

FIGURE 2. Chest computed tomographic scan after 3 months' treatment with Erlotinib.

which are commonly seen with this class of drug. After 3 months' treatment, however, she did find it necessary to "trim" her eyelashes, which were overgrowing and causing

Department of Medical Oncology, Northern Ireland Cancer Centre, Belfast. Northern Ireland.

Address for correspondence: Judith Carser, Department of Medical Oncology, Cancer Centre, Belfast City Hospital, Lisburn Road, Belfast BT9 7AB, Northern Ireland. E-mail: judith.carser@bch.n-i.nhs.uk

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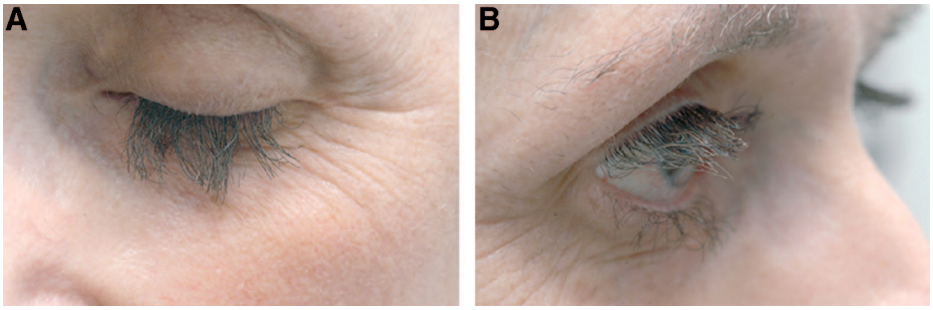

FIGURE 3. Excessive eyelash growth after 8 months of treatment.

visual disturbance and corneal irritation (Figure 3). In addition to excessive growth, her eyelashes became dark and coarse, whereas her scalp hair was fine and brittle.

DISCUSSION

Hypertrichosis of the eyelashes, known as trichomegaly, is seen in a number of congenital and acquired conditions, such as HIV-1 infection, for which it has been postulated as a clinical marker of disease severity. Trichomegaly is also associated with drugs such as phenytoin, cyclosporin, diazoxide, minoxidil, streptomycin, penicillamine, interferon 2α, and latanoprost.

There have also been case reports of trichomegaly with the EGFR inhibitors cetuximab and gefitinib.[1,2]

The cutaneous toxicity of the EGFR tyrosine kinase inhibitors is seen as a class effect and commonly includes an acneiform skin eruption, xerosis, paronychia, hyperpigmentation, and telangiectasia, as well as hair changes—of which trichomegaly is characteristic. EGFR expression and activation occurs in the basal epidermal cells, sebaceous glands, and outer root sheath of hair follicles and is necessary to stimulate the proliferation, differentiation, and survival of keratinocytes.[3]

The pathogenesis of these symptoms is largely unknown, but there is evidence that this is directly linked to inhibition of the EGFR. Cutaneous effects develop regardless of whether the inhibition is by a monoclonal antibody (cetuximab) or by a small molecule tyrosine kinase inhibitor (gefitinib, erlotinib). Cutaneous effects, however, are not seen with inhibition of other members of the EGFR family, such as Her-2 blockade with trastuzumab. There is some evidence that tumor response correlates with the presence of skin rash, and there is also a probable relationship between dose and severity of rash. This has led to increased interest in the use of cutaneous toxicity as a potential clinical marker of response, and the idea of "dose-to-rash" is ongoing in clinical trials.

As the use of the EGFR tyrosine kinase inhibitors continues to expand in non-small cell lung cancer, so our search to identify those most likely to derive clinical benefit becomes more common. Several factors, such as female sex, never smokers, adenocarcinomas (particularly bronchoalveolar), and Asian origin, are established as positive predictive markers for clinical benefit. Research into EGFR tyrosine kinase binding domain mutations forms an important part of ongoing clinical trials;[4] however, there are no published prospective data, with previous results confined to retrospective analysis from small numbers of patients for whom tissue samples are available. At present, there is insufficient information to suggest that EGFR inhibitors should be confined to any patient group.

SUMMARY

A characteristic acneiform skin rash is proving to be a useful clinical tool, and other less common cutaneous toxicities, such as isolated trichomegaly, may be similarly useful.

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